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EXAMINER	
RAILEY, J	
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Kolman 408-4253

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 13 (15) are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been canceled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 13 (15) are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☒ been filed in parent application, serial no. 08/154,930; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

Applicant's arguments with respect to claim 13 have been considered but are deemed to be moot in view of the new grounds of rejection.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing adequately to teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Applicant discloses the complete nucleic acid sequence of the genome of LAV, now known as a specific isolate of HIV-1. The sequence is translated into each of three potential reading frames in order to locate all significant open reading frames and assign gene locations. Applicant's claims are drawn to a cloned nucleic acid having a specific nucleotide sequence designated ORF-R, from position 8249 to position 8896. See page 12, last line of the specification as filed. Pages 13-16 set forth uses for the identified nucleic acid sequence. Essentially, the specification holds that the nucleic acid sequence of

ORF-R can be isolated and expressed by recombinant DNA technology to produce a protein. Alternatively, the specification holds that ORF-R can be used as a nucleic acid probe to detect HIV-1. However, the specification as filed does not set forth how to make and use the invention for the asserted purposes. The specification does not set forth the conditions for expression of ORF-R, nor whether any protein produced by expression of ORF-R has any use in the art. As noted in the previous office action, paper No. 11, mailed 17 May 1994, Brown et al. [U.S. Patent 5,001,230] describes several of the factors that must be considered for successful expression of a given gene sequence. In this regard, the expression system chosen can affect the protein produced. Prokaryotic systems do not glycosylate the protein, or may not process and fold the protein in the manner of a naturally HIV-1 infected host cell. Not all eukaryotic expression systems are alike either. This is an important point in regard to use of the expressed protein. As the specification does not identify any properties of the specific protein expressed by ORF-R, it is unclear what the skilled artisan is trying to achieve, or should be cautioned against, in expressing the protein by recombinant means. For example, if the ORF-R protein is not naturally glycosylated, yet possesses glycosylation sites, will a given expression system produce a glycosylated, i.e. non-natural, protein? See U.S. Patent No. 5,221,610 at column 6,

lines 35-36. In addition, to have any particular use as a diagnostic the ORF-R expressed by recombinant means in a particular host cell would have to generate a protein specifically recognized by sera or activated T cells of an HIV-1 infected individual. As noted in U.S. patent 5,221,610, patient infected with HIV-1 produce antibodies to ORF-R protein. [See column 6, lines 24-34.] This fact is not evident in the specification as filed. Is the presence of such antibodies consistently detectable using the expressed protein as a diagnostic? It is not evident which, if any, recombinantly expressed ORF-R proteins would have those same properties as the naturally produced protein. This is also an important point especially in regard to the specification's asserted use of ORF-R protein in a vaccine. The specification provides no evidence that ORF-R protein alone, or in combination with other antigens, is useful as a vaccine. HIV-1 has so far resisted all attempts at developing vaccines or therapeutics based upon recombinant expression of antigens. See Haynes [Science 260:1279-1286 (1993)]. Applicant's specification is based upon a 1984 priority and contains a wish that vaccines or therapeutics might be developed from expression of HIV-1 antigens. This is not an enabled use for the invention as claimed.

Alternatively, the specification holds that ORF-R can be used as a nucleic acid probe to detect HIV-1. The specification however does

not demonstrate this use. It is not demonstrated that the nucleic acid hybridizes specifically with HIV-1 to detect the presence or absence of this virus in a biological sample. No specific conditions or methods are given which would allow discrimination between HIV-1 and other retroviruses such as HTLV-I or HTLV-II, or other lentiviruses such as SIV or HIV-2 when using the claimed probe. How specific is the probe for any given variant of HIV-1; will it detect strains other than LAV? How are these various "biological samples" to be prepared for the hybridizations such that HIV-1 is detected specifically, reproducibly and accurately? Applicant has provided a reference by Arya et al. [Science 225:927-930 (1984)], Exhibit 4, which shows that the region between the env gene and the 3'LTR does hybridize to members of the HTLV family. See the abstract as well as page 929, first column. Cross-hybridization was also shown in Hahn et al. [Nature 312:166-169 (1984)]. Consequently, the instant specification would have to set forth specific hybridization conditions which would allow discrimination between these viruses if ORF-R is used as a probe. It does not. In addition, as applicant notes in their response, paper No. 13, received 16 August 1994, ORF-R does have homology to a corresponding region in HIV-2. Hybridization conditions to distinguish these two viruses using applicant's ORF-R as a probe are similarly not set forth. Given the lack of guidance in

the specification as filed, as well as the established fact that cross-hybridization does occur, it would require undue experimentation by the skilled artisan to establish such conditions. Consequently, the specification as filed fails to teach how to make and use the invention as disclosed.

Claim 13 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Art Unit 1804 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for Art Unit 1804 is (703) 308-4312.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. F. Railey, whose telephone number is (703) 308-0281. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jacqueline Stone, can be reached at (703) 308-3153. The fax phone number for Art Unit 1804 is (703) 308-4312.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JACQUELINE M. STONE
SUPERVISORY PATENT EXAMINER
GROUP 1800

Johnny F. Railey II, Ph.D.
March 2, 1995